

**In the Claims:**

This listing of claims will replace all prior versions and listings of the claims in this application.

**Listing of Claims**

1. (Currently Amended) A nucleic acid construct comprising a nucleic acid sequence further comprising a ~~reporter gene~~ nucleic acid sequence encoding a reporter protein that is secretable or excretable as a protein or product from a cell where ~~it~~ the protein or product is expressed or produced ~~and that is excretable from a whole animal the construct further comprising a peptide tag.~~
2. (Currently Amended) [[A]] The nucleic acid construct according to claim 1, wherein the secretable/excretable protein or product is produced by modulated gene transcription.
3. (Currently Amended) [[A]] The nucleic acid construct according to claim 1, wherein the secretable/excretable protein or product is produced by increased reporter translation.
4. (Currently Amended) [[A]] The nucleic acid construct according to claim 3, wherein the increased reporter translation is [[as]] a result function of increased stability or decreased turnover of mRNA.
5. (Currently Amended) [[A]] The nucleic acid construct according to claim 1, wherein the secretable/excretable protein or product is produced by post-translational modulation.
6. (Currently Amended) [[A]] The nucleic acid construct according to claim 5, wherein the post-translational modulation is increased reporter stability through removal of polyubiquination or [[as]] a function ~~the result~~ of accumulation or excretion of small molecule metabolites.

7. (Currently Amended) ~~[[A]]~~ The nucleic acid construct according to ~~any preceding claim 37, further comprising a wherein the~~ peptide tag ~~optionally in the form of~~ further comprises an epitope tag or a tag comprising enzymatic activity.

8. (Currently Amended) ~~[[A]]~~ The nucleic acid construct according to ~~any preceding claims additionally claim 37 further~~ comprising a promoter element upstream of the (i) ~~[[a]]~~ the nucleic acid sequence encoding a the secreted/excreted protein, and/or (ii) a nucleic acid sequence encoding ~~[[a]]~~ the peptide tag.

9. (Currently Amended) ~~[[A]]~~ The nucleic acid construct according to ~~any preceding claim 1,~~ wherein the secreted/excreted reporter protein is secreted alkaline phosphatase (SEAP).

10. (Currently Amended) ~~[[A]]~~ The nucleic acid construct according to claim 9, wherein the construct further ~~includes~~ comprises a CypA1 promoter.

11. (Currently Amended) ~~[[A]]~~ The nucleic acid construct according to ~~any of claims 1 to 8 claim 1,~~ wherein the secreted/excreted reporter protein is a modified human  $\beta$  choriogonadotrophin (hCG) molecule.

12. (Currently Amended) ~~[[A]]~~ The nucleic acid construct according to claim 11, wherein the construct further ~~includes~~ comprises a stratifin gene promoter.

13. (Currently Amended) ~~[[A]]~~ The nucleic acid construct according to ~~either claim 11, or 12~~ wherein the hCG molecule is tagged.

14. (Currently Amended) ~~[[A]]~~ The nucleic acid construct according to claim 13, wherein the hCG molecule is myc-tagged.

15. (Currently Amended) [[A]] The nucleic acid construct according to ~~any of claims 1 to 8~~ claim 1, wherein the secreted/excreted reporter protein/product is selected from the group ~~comprising~~ consisting of hormonal molecules, antibodies and enzymatic molecules.

16. (Currently Amended) [[A]] The nucleic acid construct according to claim 15, wherein the hormonal molecule is FSH.

17. (Currently Amended) [[A]] The nucleic acid construct according to claim 15, wherein the antibody is a  $\gamma$  or light chain (Bence Jones) protein.

18. (Currently Amended) [[A]] The nucleic acid construct according to claim 15, wherein the enzymatic molecule is feline urinary carboxylase.

19. (Currently Amended) A host cell ~~transfected with~~ comprising at least one nucleic acid construct according to ~~any one of claims 1 to 18~~ claim 1.

20. (Currently Amended) A cell line ~~transfected with~~ comprising at least one nucleic acid construct according to ~~any one of claims 1 to 18~~ claim 1.

21. (Currently Amended) A transgenic non-human animal ~~in which~~ wherein the cells of the non-human animal express the protein or product encoded by the nucleic acid sequence of the nucleic acid construct according to ~~any one of claims 1 to 18~~ claim 1.

22. (Currently Amended) [[A]] The transgenic non-human animal according to claim 21, ~~in which~~ wherein the non-human animal is a mammal.

23. (Currently Amended) [[A]] The transgenic non-human mammal according to claim 22, ~~in which~~ wherein the mammal is a mouse.

24. (Currently Amended) ~~[[A]]~~ The transgenic non-human animal according to ~~any one of claims 21 to 23~~ claim 21, wherein the secreted/excreted reporter ~~product or~~ protein or product molecule is excreted in a body fluid selected from the group ~~comprising~~ consisting of urine, saliva, tears, milk, cerebrospinal fluid and semen.

25. (Currently Amended) ~~[[A]]~~ The transgenic non-human animal according to ~~any one of claims 21 to 24~~ claim 21, wherein the secreted/excreted reporter ~~product or~~ protein or product molecule is excreted in urine.

26. (Currently Amended) ~~[[A]]~~ The host cell according to claim 19, ~~or a cell line according to claim 20 or a transgenic non-human animal according to any one of claims 21 to 25~~ wherein the secreted/excreted reporter moiety ~~is of relatively low~~ protein or product has a molecular weight~~[[,]] in the region of < of about less than~~ 60-120kDa.

27. (Currently Amended) ~~[[A]]~~ The host cell according to claim 19, ~~or a cell line according to claim 20 or a transgenic non-human animal according to any one of claims 21 to 25~~ wherein the secreted/excreted reporter moiety ~~possesses~~ protein or product comprises a hydrophilic globular tertiary structure, ~~has~~ low bio-activity ~~[[is]]~~ and/or is ~~clearly~~ distinguishable from ~~native endogenous~~ molecules ~~so that it is readily detectable and quantifiable~~.

28-30. (Canceled)

31. (Currently Amended) A method of detecting a gene activation event in a cell *in vitro* or *in vivo*, comprising assaying a host cell ~~stably transfected with~~ or transgenic non-human animal ~~each comprising~~ a nucleic acid construct ~~in accordance with any one of claims 1 to 18 according to claim 1, or a transgenic non-human animal according to any one of claims 21 to 25, in which~~ wherein the cell or animal is subjected to a gene activation event that is signalled by expression of a secreted/excreted reporter protein wherein optionally the protein being is optionally tagged with an epitope.

32. (Currently Amended) A method of screening for, or monitoring of, toxicologically induced stress in a cell or a cell line or a non-human animal, comprising ~~the use of evaluating a cell, cell line or non human animal which has been transfected with or carries a~~ each comprising the nucleic acid construct according to any one of claims 1 to 18 claim 1.

33. (Currently Amended) A method for screening and ~~characterising~~ characterizing viral, bacterial, fungal, and parasitic infection or ~~for~~ screening for cancer, inflammatory disease, cardiovascular disease, metabolic disease, neurological disease and disease with a genetic basis comprising ~~the use of evaluating a cell, cell line or non human animal which has been transfected with or carries a~~ each comprising the nucleic acid construct according to any one of claims 1 to 18 claim 1.

34. (New) The nucleic acid construct according to claim 1, wherein the reporter protein is expressed or produced in vitro or in vivo.

35. (New) The nucleic acid construct according to claim 1, wherein the reporter protein is secretable/excretable from a whole animal.

36. (New) The nucleic acid construct according to claim 35, wherein the whole animal is a transgenic non-human animal.

37. (New) The nucleic acid construct according to claim 1, wherein the construct further comprises a peptide tag.

38. (New) A reporter system comprising at least two nucleic acid constructs, wherein the nucleic acid constructs each comprise:

- (i) a nucleic acid sequence encoding a reporter protein; and
- (ii) a nucleic acid sequence encoding a peptide tag to the reporter protein,

wherein each reporter protein is distinct from the proteins normally expressed in the host comprising the reporter system.

39. (New) The reporter system according to claim 38, wherein the at least two nucleic acid constructs encode a same reporter protein having a different peptide tag or encode a different protein having a same peptide tag.

40. (New) The reporter system according to claim 38, wherein the reporter protein is selected from the group consisting of secreted alkaline phosphatase (SEAP), a  $\gamma$  or light chain (Bence Jones) protein and feline urinary carboxylase.